

The predicted initiating methionine (Kozak, M., *Nucleic Acids Res.* 12:857-872, 1984) and signal peptide (Heijne, G.v., *Nucleic Acids Res.* 14:4683-4690, 1986) are underlined. Although preceded by two putative methionine codons at bases 124 and 226, these codons are followed by in-frame stop codons after 4 and 59 amino acids, respectively. In addition, they are surrounded by weak consensus sequences for initiation sites, while the proposed initiating methionine comprises a strong initiation sequence (Kozak, M., *Nucleic Acids Res.* 12:857-872, 1984) preceded by an in-frame stop codon. The putative transmembrane domain is underlined, the potential N-glycosylation sites boxed and the conserved extracellular cysteines are circled. Key amino acids of the catalytic domain of MDK1 are highlighted in bold italics. The polyadenylation motif (AATAAA) (SEQ. I.D. NO. 7) is underlined, the alternative 3'-untranslated region of MDK1 is given below.

Figure 2 shows the overview of various forms of MDK1 RTKs. Figure 2A shows the nucleotide sequence of MDK1.T1 (as set forth in SEQ ID NO: 4) beginning with nucleotide 1913, and Figure 2B shows the nucleotide sequence of MDK1.T2 (as set forth in SEQ ID NO: 6) beginning with nucleotide 1913. The divergent sequence due to alternative splicing is shown underlined, as is the polyadenylation motif (AATAAA) (SEQ I.D NO: 8) in the sequence of MDK1.T1.

Figure 2C shows a schematic representation of MDK1 and its variants. The open reading frame is indicated by boxes, the untranslated regions of the MDK1 sequences are given in bold lines. Below, the amino acid sequence variations in the marked region of the different forms of MDK1 are shown. The missing nucleotide stretches are indicated (---). The sequences shown each begin at amino acid residue number 535 in MDK1 (SEQ ID NO: 2), MDK1.T1 (SEQ ID NO: 3), MDK1.T2 (SEQ ID NO: 5), MDK1.Δ1 (SEQ ID NO: 11), and MDK1.Δ2 (SEQ ID NO: 12).

Figure 3 is a dendrogram for the eck/eph subfamily of RTKs. The predicted protein sequences of MDK1, Hek2 (Böhme et al., 1993), Cek6, 7, 8, 9 and 10 (Sajjadi and Pasquale, *Oncogene* 8:1807-1813, 1993), Elk (Lhotak et al., *Mol. Cell. Biol.* 11:2496-2502, 1991), Cek5 (Pasquale, E.B., *Cell Regula.* 2:523- 534, 1991), Mek4, Cek4 (Sajjadi et al., *New Biol.* 3:769-778, 1991 ), Hek (Wicks et al., *Proc. Natl. Acad. Sci. USA*

89:1611-1615, 1992.), Ehk1, Ehk2 (Maisonneuve et al., *Oncogene* 8:3277-3288, 1993), Sek (Gilardi-Hebenstreit et al., *Oncogene* 7:2499-2506, 1992), Eek (Chan and Watt, *Oncogene* 6:1057-1061, 1991), Eck (Lindberg and Hunter, *Mol. Cell. Biol.* 10:6316-6324, 1990) and eph (Hirai et al., *Science* 238:1717-1720, 1987) were aligned using progressive, pairwise alignments according to the method of Higgins and Sharp (Higgins and Sharp, *CABIOS* 5:151-153, 1989). Published sequence data for erk (Chan and Watt, *Oncogene* 6:1057-1061, 1991) and tyro1, 4, 5, 6 and 11 (Lai and Lemke, *Neuron* 6:691-704, 1991) were insufficient for inclusion in the analysis. A tree of sequence similarity generated by use of the Unweighted Pair Group Method with Arithmetic mean algorithm (UPGMA; Sneath and Sokal, in Numerical Taxonomy, W.H. Freeman and Company, San Francisco, 1973, pp. 230-234) calculated on basis of the multiple alignment is shown.)--

On page 94, please replace the first paragraph of Example 2 with the following:

[2] Northern blot analysis was performed with different nucleotide probes of the MDK1 and MDK1.T1 cDNA. 4 µg of poly(A<sup>+</sup>) RNA isolated from 13.5 day mouse embryos were analyzed. Sizes were determined by using the residual 28S and 18S ribosomal RNAs as internal markers and are indicated by arrowheads. The probes used correspond to nucleotides 282-1847 (A), 1847-2082 (B), 2029-2900 (C) and 3758-4304 (D) of MDK1 (as set forth in SEQ ID NO: 1) and nucleotides 2044-2666 (E) of MDK1.T1 (as set forth in SEQ ID NO: 3). Using the extracellular domain of MDK1 as a probe, we identified five transcripts of 6.8, 5.7, 4.0, 3.2, and 2.6 kb in poly(A<sup>+</sup>) RNA from mouse embryo day 13.5 p.c. The two smallest transcripts were also detected with a probe corresponding to the transmembrane domain, but not with a probe corresponding to the intracellular domain of MDK1, confirming the existence of transcripts encoding variant forms of MDK1 lacking the intracellular kinase domain found by the cDNA library screening. The 3.2 kb transcript corresponds to MDK1.T1, whereas the lowest band probably corresponds to MDK1.T2, since the size of 2.6 kb matches that of the cDNA of MDK1.T2. The upper three bands of 6.8, 5.7, and 4.0 kb are predicted to encode the full-length MDK1 forms, with the 6.8 kb and 5.7 kb transcripts resulting from the use of an alternative polyadenylation site.)--

Claim 4. (Twice amended) A recombinant nucleic acid, comprising:

a transcriptional region functional in a cell[, a sequence complementary to an RNA sequence] comprising a nucleic acid sequence that, when transcribed, produces a transcript

(a) encoding a MDK1 polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 2; or

(b) that [hybridizes under stringent conditions] is complementary to the nucleic acid of (a); and

a translational termination region functional in a cell.

Claim 16. (Twice amended) The isolated, enriched, or purified nucleic acid of claim 1 comprising [a] the nucleic acid sequence set forth in SEQ ID NO: 1.

Claim 18. (Twice amended) The isolated, enriched, or purified nucleic acid of claim 19 comprising a nucleic acid sequence of SEQ ID NO: [3] 4 or SEQ ID NO: [4] 6.

Claim 19. (Twice amended) An isolated, enriched, or purified nucleic acid

(a) encoding MDK1.T1 set forth in SEQ ID NO:3; MDK1.T2 set forth in SEQ ID NO:5; MDK1.Δ1 set forth in SEQ ID NO:11; [and] or MDK1.Δ2 set forth in SEQ ID NO:12; or

(b) that is complementary to the nucleic acid of (a).

Claim 21. (Three times amended) An isolated, enriched, or purified nucleic acid

(a) [comprising a nucleic acids sequence of claim 1] encoding [the] a MDK1 polypeptide comprising the extracellular domain as set forth [as shown] by amino acids 18 to 538 of [Figure 1] SEQ ID NO: 2; or

(b) that is complementary to the nucleic acid of (a).